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## Evaluation of several multiple diglycolamide-functionalized calix[4]arene ligands for the isolation of carrier free $^{90}\text{Y}$ from $^{90}\text{Sr}$

P.K. Mohapatra <sup>a,\*</sup>, D.R. Raut <sup>a</sup>, M. Iqbal <sup>b</sup>, J. Huskens <sup>b</sup>, W. Verboom <sup>b</sup><sup>a</sup> Radiochemistry Division, Bhabha Atomic Research Centre, Trombay, Mumbai-400085, India<sup>b</sup> Laboratory of Molecular Nanofabrication, MESA<sup>+</sup> Institute for Nanotechnology, University of Twente, PO Box 217, 7500 AE Enschede, The Netherlands

### HIGHLIGHTS

- $^{90}\text{Y}$  separation was attempted from  $^{90}\text{Sr}$  using solvent extraction.
- DGA-functionalized calixarenes were used as extractants.
- Separation factors in the excess of  $10^6$  were obtained.
- The purity of the product was ascertained by half-life method.

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### ABSTRACT

Several diglycolamide-functionalized calix[4]arenes containing four and eight diglycolamide (DGA) moieties were evaluated for their relative extraction efficiencies towards Y(III) and Sr(II). Ligands containing four DGA units with *n*-propyl, iso-pentyl, and *n*-octyl groups at the amidic N atom adjacent to the calix[4]arene skeleton showed efficient extraction of Y(III) from 3 M HNO<sub>3</sub>. The extraction of Sr(II) was poor in all cases in the entire acidity range (0.1–6 M HNO<sub>3</sub>) studied. The ligands with a hydrogen atom and an *n*-propyl group at the concerning amidic N atom showed a very high separation efficiency as reflected in separation factor (S.F. =  $D_Y/D_{Sr}$ ) values in the range of  $10^5$ – $10^6$ . A method was developed for the separation of carrier-free  $^{90}\text{Y}$  from a  $^{90}\text{Y}$ - $^{90}\text{Sr}$  mixture involving consecutive extraction–stripping cycles. The product purity was checked using half-life measurements. Two consecutive cycles of extraction and stripping were found to be sufficient for obtaining pure  $^{90}\text{Y}$ . The results obtained in the present studies were compared with those obtained previously using analogous ligands such as TODGA (*N,N,N',N'*-tetraoctyl diglycolamide), T2EHDGA (*N,N,N',N'*-tetra-2-ethylhexyl diglycolamide), and PC-88A (bis(2-ethylhexyl) phosphonic acid).

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## 1. Introduction

$^{90}\text{Y}$  based radiopharmaceuticals are widely used for the treatment of cancerous tissues in targeted therapy. Ideal characteristics of  $^{90}\text{Y}$  such as short half-life ( $t_{1/2}$  = 64.1 h) and high energy radiations ( $\beta$ -max = 2.2 MeV) make it one of the most suitable radioisotopes for radiopharmaceutical applications (Ferrari et al., 2006; Kaltsas et al., 2005).  $^{90}\text{Y}$  can be prepared by irradiation of  $^{89}\text{Y}$  in a nuclear reactor. Though the radionuclide purity of the activated  $^{90}\text{Y}$  is very high, the low neutron absorption cross section of  $^{89}\text{Y}$  (0.001 b) makes the product with very low specific activity (Qaim, 2001). Alternatively, carrier-free  $^{90}\text{Y}$  is a better option and is often required for targeted therapy using DOTA type complexes (Barone et al., 2005). The tracer

can be obtained by separation of  $^{90}\text{Y}$  from  $^{90}\text{Sr}$ , which contains the former as its daughter product in a secular equilibrium (IAEA, 2009). In view of the large half-life of  $^{90}\text{Sr}$  ( $t_{1/2}$  = 28.5 yr),  $^{90}\text{Y}$  can be separated from the parent source whenever the need arises and it can act as a generator similar to the  $^{99}\text{Mo}$ - $^{99m}\text{Tc}$  generator.  $^{90}\text{Sr}$  is one of the most abundant fission product radionuclides in spent nuclear fuel as it is generated during the fission reaction in high yield. Therefore, nuclear waste is the biggest source of  $^{90}\text{Sr}$  and there are efforts to recover this important radionuclide (Schulz and Bray, 1987). Furthermore, the development of an efficient method for the separation of  $^{90}\text{Y}$  from  $^{90}\text{Sr}$  is a challenging task. It is well known that  $^{90}\text{Sr}$  is a bone seeker and the maximum permissible body burden of this radionuclide is 74 kBq or 2  $\mu\text{Ci}$  (NBS, 1959) and for a radiopharmaceutical containing Curie level radioactivity, decontamination factor values as high as  $10^6$  are a pre-requirement, while designing a separation process. Separation of mega curie quantities of  $^{90}\text{Y}$  is possible by developing suitable Y(III) selective molecules with very little affinity for Sr(II).

\* Corresponding author.

E-mail address: [mpatra@barc.gov.in](mailto:mpatra@barc.gov.in) (P.K. Mohapatra).

Several techniques such as solvent extraction (Wike et al., 1990; Lee and Ting, 1991), ion-exchange (Suzuki, 1964; Roy et al., 2004), extraction chromatography (Hsieh et al., 1993), precipitation (Salutsky and Kirly, 1955), liquid membrane (Ramanujam et al., 2001), etc. have been used for the separation of  $^{90}\text{Y}$  from  $^{90}\text{Y}$ – $^{90}\text{Sr}$  mixtures. The principle involved in such separation methods is either the preferential complexation of Y(III) using selective extractants like PC-88A (bis(2-ethylhexyl) phosphonic acid) and CMPO (carbamoylmethylphosphine oxide) (Dhami et al., 2007) followed by stripping/elution or preferential extraction of Sr(II) using ligands such as crown ethers (Dietz and Horwitz, 1992) leaving behind the carrier-free  $^{90}\text{Y}$  in the feed. Horwitz et al. (1992) developed a Sr specific resin (Sr-SPEC<sup>®</sup>) for the selective sorption of Sr from acidic feeds using a Sr<sup>2+</sup> ion specific crown ether, viz., di-*tert*-butyl-dicyclohexano-18-crown-6 as the extractant and 1-octanol as the diluent. The method involves loading of a mixture of  $^{90}\text{Y}$ – $^{90}\text{Sr}$  in 3 M HNO<sub>3</sub> on to a column made from Sr-Spec<sup>®</sup> resin, which holds  $^{90}\text{Sr}$ , while  $^{90}\text{Y}$  passes through. Though the product was reasonably free from  $^{90}\text{Sr}$ , it was not good enough for pharmaceutical usage. Chakravarty and Dash (2012) showed that the purity of the  $^{90}\text{Y}$  product obtained using a crown ether-containing resin in a chromatographic mode can be improved. However, the disadvantage of this method includes extensive damage of the resin due to the high energy beta particles emitted from both  $^{90}\text{Sr}$  and  $^{90}\text{Y}$ . Kandwal et al. (2011) used a liquid membrane-based separation method using PC-88A as the extractant. Though the throughput was significantly higher compared to another liquid membrane method mentioned above (Dhami et al., 2007), the product purity was not satisfactory.

Diglycolamide (DGA) ligands are reported to be highly efficient extractants for actinides and have shown a preference for the trivalent lanthanides over the trivalent actinides (Sasaki et al., 2001). On the other hand, alkali and alkaline earth metal ions such as Cs<sup>+</sup> and Sr<sup>2+</sup> are extracted to a much lower extent suggesting reasonably high decontamination from these cations. In view of the similarity in the chemical properties of trivalent lanthanides and Y<sup>3+</sup>, it was expected

to obtain a good separation of  $^{90}\text{Y}$  from  $^{90}\text{Sr}$  using diglycolamides. Dutta et al. (2011a–2011c, 2012) utilized this property to report a reasonably satisfactory separation behaviour of the metal ions using TODGA (*N,N,N',N'*-tetra-*n*-octyl diglycolamide) and *N,N,N',N'*-tetra(2-ethylhexyl) diglycolamide (T2EHGDA). These studies resulted in reasonably good decontamination factor (DF) values as seen from half-life measurements, which could be improved by fine tuning of the separation method. For example, the DF values could be made higher by increasing the number of extraction stripping stages.

Multiple diglycolamide-functionalized extractants such as tripodal diglycolamide (T-DGA, (Mohapatra et al., 2011)) and diglycolamide-functionalized calix[4]arenes (Mohapatra et al., 2012a, 2012b) not only resulted in a significant enhancement in the distribution ratio (*D*) values of the trivalent lanthanides and actinides, but also in the separation factor values, compared to TODGA. However, almost no change in the corresponding *D* values for Sr(II) was observed. This makes this class of extractants as significantly more efficient than those already known for the separation of  $^{90}\text{Y}$  from a mixture containing  $^{90}\text{Y}$  and  $^{90}\text{Sr}$ .

The present paper deals with the use of a series of DGA-functionalized calix[4]arenes (L-I–L-V, Fig. 1) for the separation of carrier-free  $^{90}\text{Y}$  from  $^{90}\text{Sr}$ . The purity of the product radionuclide was tested by the conventional half-life method. The stripping of the extracted  $^{90}\text{Y}$  was carried out using (ethylenediamine-*N,N,N',N'*-tetraacetic acid). The eluted fraction containing these strongly complexing ligands suggested their direct application as radiopharmaceuticals.

## 2. Experimental

### 2.1. Reagents

Synthesis of the DGA-functionalized calix[4]arenes L-I–L-V was carried out at following procedures described elsewhere (Iqbal et al., 2012). The ligands were characterized by NMR, IR, and ESI-MS and were also used for obtaining metal ion distribution ratio values reported earlier (Iqbal et al., 2012), which was an indirect method of testing the purity. 99% Pure *n*-dodecane (Lancaster) and isodecanol (Fluka) were used as received. All the other reagents were of AR grade and were used without further purification. Suprapur nitric acid (Merck) was used for the preparation of dilute nitric acid solutions using milli-Q water (Millipore).

$^{90}\text{Y}$  tracer studies were carried out using a stock solution of the radionuclide obtained by the neutron activation of 99.99% pure Y<sub>2</sub>O<sub>3</sub>, which was subsequently dissolved in suprapur nitric acid and diluted with deionized water.  $^{85,89}\text{Sr}$  tracer was procured from BRIT, Mumbai, and was used as a surrogate for  $^{90}\text{Sr}$ .  $^{90}\text{Y}$  was assayed by beta counting using a liquid scintillation counting system (Hydex, Finland) using a toluene-based scintillator cocktail (Sisco Research Laboratory, Mumbai), while the assaying of  $^{85,89}\text{Sr}$  was done by gamma counting using a well type NaI(Tl) scintillation counter (Para Electronics, India) inter phased to a multi-channel analyzer (ECIL), respectively.

### 2.2. Solvent extraction studies

The solvent extraction studies were carried out by vortexing Pyrex glass tubes containing equal volumes (usually 1 mL) of the tracer spiked (either  $^{90}\text{Y}$  or  $^{85,89}\text{Sr}$ ) aqueous phase at the desired acidity with the organic phase containing the DGA-functionalized calix[4]arene extractants L-I–L-V in a 95% *n*-dodecane + 5% isodecanol diluent mixture in a rotary thermostated water bath for an hour at 25.0 ± 0.1 °C. Subsequent to agitation, the tubes were centrifuged and assayed by taking suitable aliquots (usually 100 μL) from both phases. Typically, the concentration of both Y(III) and Sr(II) was in the range of 10<sup>−4</sup>–10<sup>−5</sup> M. The distribution

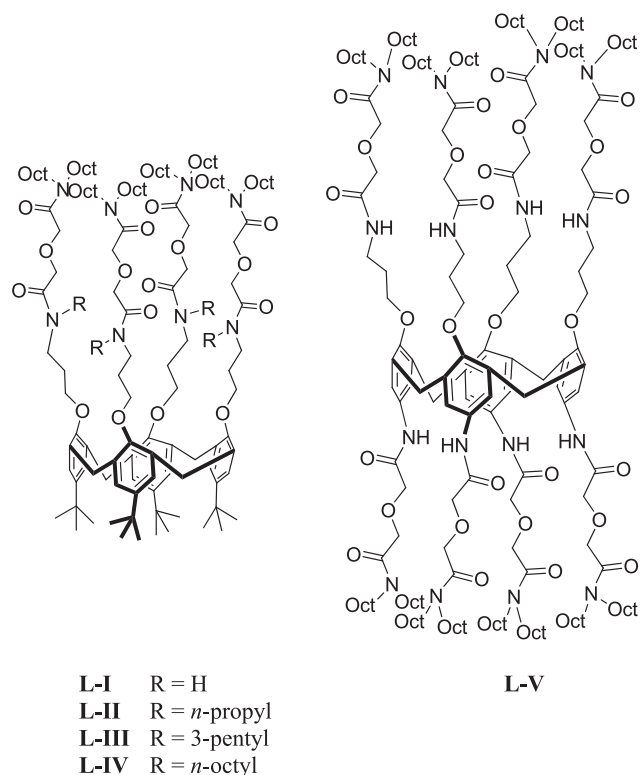


Fig. 1. Structures of DGA-functionalized calix[4]arene ligands L-I: R=H; L-II: R=*n*-propyl, L-III: R=3-pentyl, L-IV: R=*n*-octyl, and L-V.

ratio of the metal ion ( $D_M$ ) is defined as the ratio of the activity (counts per minute) of the tracer per unit volume in the organic phase to that in the aqueous phase. The separation factor (S.F.) is defined as the ratio of  $D_Y$  to  $D_{Sr}$ , while the decontamination factor is defined as the ratio of the ratio of concentration of Y to Sr in the product to that in the feed solution. Half-lives were measured by following the activity of the product as a function of time over several days. All solvent extraction experiments were carried out in duplicate and the distribution ratio ( $D_M$ ) data represent the average of the two results. The material balance in all the Y(III) experiments was within an error limit of  $\pm 5\%$ , while the data involving Sr(II) had an error limit of  $\pm 2\%$ .

### 3. Results and discussion

Since some of the DGA-functionalized calix[4]arene ligands have a poor solubility in pure *n*-dodecane prompted us to use a mixture of 95% *n*-dodecane + 5% iso-decanol. This diluent mixture has been used by us in earlier studies involving actinide ion extraction (Gujar et al., 2010a). In studies involving TODGA and T2EHDGA as the extractants, this diluent composition has been used with good results for possible actinide partitioning runs (Gujar et al., 2010b, 2012). We have used a solution of T2EHDGA in an *n*-dodecane–iso-decanol mixture to get a purer form of  $^{90}\text{Y}$  from  $^{90}\text{Sr}$  as compared to a solution in chloroform (Dutta et al., 2012).

#### 3.1. Effect of the feed nitric acid concentration

The separation efficiency of  $^{90}\text{Y}$  from its parent radionuclide ( $^{90}\text{Sr}$ ) has been reported to be dependent on the feed acid concentration. Such behaviour was previously reported (Kandwal et al., 2011) using PC-88A (an acidic extractant) as the Y(III) selective ligand. Acid concentration dependent separation efficiency was seen in separate reports with both TODGA as well as T2EHDGA (Dutta et al., 2011a, 2011b). Apparently, the extraction of both Y(III) and Sr(II) varies with the nitric acid concentration, though not to the same extent resulting in high separation factor values at both 1 M as well as 6 M  $\text{HNO}_3$  (Dutta et al., 2011a).

The extraction profiles of Y(III) were obtained from aqueous feed solutions containing 0.01–6 M  $\text{HNO}_3$  with the DGA-functionalized calix[4]arenes L-I–L-V and the data are presented

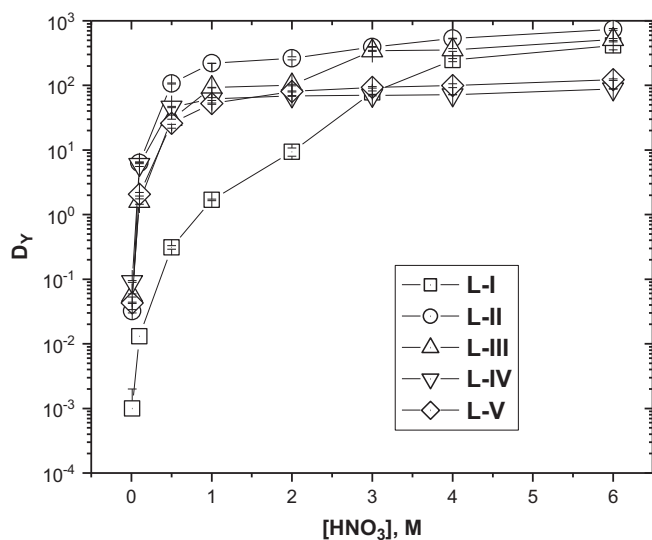


Fig. 2. Effect of feed acidity on Y(III) uptake by DGA-functionalized calix[4]arene ligands L-I–L-V; [Ligand] =  $1.0 \times 10^{-3}$  M, equilibration time: 1 h.

Table 1  
Y(III) extraction data with  $1.0 \times 10^{-3}$  M DGA-functionalized calix[4]arene ligands L-I–L-V.

Ligand	$D_Y$		Slopes of $\log D_Y$ vs $\log [L]$ plots obtained at 3 M $\text{HNO}_3$
	2 M $\text{HNO}_3$	3 M $\text{HNO}_3$	
L-I	$9.36 \pm 1.31$	$77.5 \pm 4.4$	$2.21 \pm 0.02$
L-II	$263 \pm 14$	$394 \pm 6$	$1.62 \pm 0.03$
L-III	$102 \pm 2.8$	$343 \pm 14$	$2.30 \pm 0.04$
L-IV	$68.8 \pm 0.9$	$70.6 \pm 1.5$	$0.76 \pm 0.05$
L-V	$80.8 \pm 1.5$	$93.1 \pm 2.5$	$0.95 \pm 0.03$

graphically in Fig. 2. In all cases, the extraction increased with increased aqueous phase acid concentration, though the shapes of the profiles are different. While a slow initial increase in Y(III) extraction at lower acidities which changed to a rather sharp increase in the  $D_Y$  values beyond 0.5 M  $\text{HNO}_3$  was seen in case of L-I, a faster increase followed by plateau-like profiles were observed in case of the rest of the ligands (Fig. 2). Further, at 2–3 M  $\text{HNO}_3$  (Table 1), relatively higher Y(III) extraction was observed for L-I, L-II, and L-III as compared to L-IV and L-V. L-II gave rise to higher  $D_Y$  values than the other extractants in the major part of the acidity range investigated. The extraction trend of the DGA-functionalized ligands L-I–L-V at 3 M  $\text{HNO}_3$  was as follows: L-II > L-III > L-V > L-I > L-IV, while it was L-II > L-III > L-V > L-IV > L-I at lower than 2 M  $\text{HNO}_3$ , suggesting the role of the nitric acid concentration on the relative extraction efficiencies of the ligands. The extraction of nitric acid by the ligands was found to be negligible using a reported method on volumetric titrations of the organic phase using phenolphthalein indicator (Gujar et al., 2010a). In view of low concentrations of the ligand, even 1:1 or 1:2 species formation with L and  $\text{HNO}_3$  (as  $L \cdot \text{HNO}_3$  or  $L \cdot 2\text{HNO}_3$ ) are expected not to affect the extraction equilibrium significantly and hence, are ignored hereafter.

At 0.01 M  $\text{HNO}_3$ , L-II to L-V yielded  $D_Y$  values in the range of 0.03–0.1, which are reasonably low as compared to the metal ion extraction at higher acidities suggesting that the metal ion can be stripped by equilibrating with a pH 2 solution. The most efficient stripping data at pH 2 as the aqueous phase can, however, be obtained with L-I as the extractant (Fig. 2). At least till about 2 M  $\text{HNO}_3$  (see Fig. 2) the substituents at the amidic nitrogen atoms in ligands L-II–L-IV give rise to higher extraction efficiency compared to that of L-I. This may be caused by the higher basicity, better lipophilicity, and steric reasons as outlined before for actinide/lanthanide extraction (Iqbal et al., 2012).

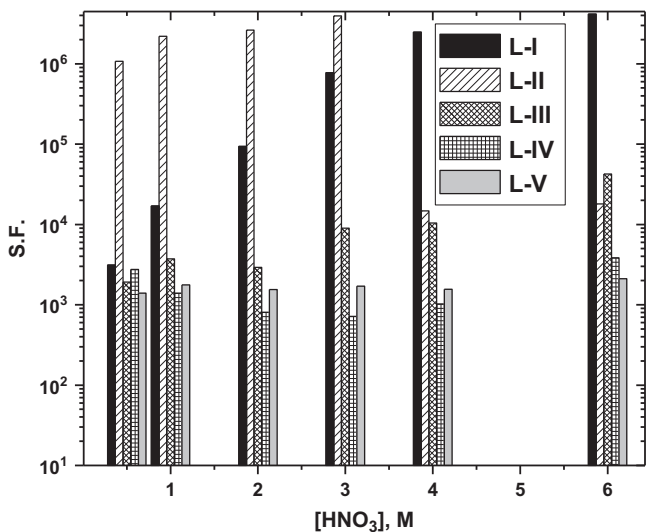
Though it is known that Sr(II) extraction is rather low as compared to the extraction of trivalent lanthanides and actinides, it was of interest to study the extraction behaviour of the DGA-functionalized calix[4]arenes L-I–L-V. Table 2 lists the Sr(II) extraction data which are unusually low ( $< 10^{-4}$ ), particularly for L-I and L-II, while the  $D_{Sr}$  values of the other extractants (L-III to L-V) are more than two orders of magnitude larger. This implies that the most impressive separation factor (S.F., defined as  $D_Y/D_{Sr}$ ) values were obtained with ligands L-I and L-II being as large as  $\sim 4 \times 10^6$  (Table 3). Similar large separation factors have been reported in literature while using crown based extractants (Vanura and Jedináková-Krízová, 2003; Makrlík and Vanura, 2008). We have previously carried out studies with other DGA ligands such as TODGA and T2EHDGA which, though have shown favourable extraction for Y(III) as compared to Sr(II), did not appear as promising as these multiple DGA-functionalized ligands used in the present study. A graphical representation of the separation factor data is shown in Fig. 3. As shown in Table 4, These S.F. values are about two orders of magnitude larger than those obtained with TODGA (Dutta et al., 2011a) and four orders of magnitude higher than

**Table 2**  
Effect of feed acidity on Sr(II) uptake by  $1.0 \times 10^{-3}$  M DGA-functionalized calix[4] arene ligands L-I–L-V. O/A:1, equilibration time: 60 min.

HNO <sub>3</sub> , M	L-I	L-II	L-III	L-IV	L-V
0.01	< 10 <sup>-4</sup>	< 10 <sup>-4</sup>	< 10 <sup>-4</sup>	< 10 <sup>-4</sup>	0.014 ± 0.001
0.1	< 10 <sup>-4</sup>	< 10 <sup>-4</sup>	0.005 ± 0.000	< 10 <sup>-4</sup>	0.016 ± 0.000
0.5	< 10 <sup>-4</sup>	< 10 <sup>-4</sup>	0.016 ± 0.002	0.017 ± 0.001	0.019 ± 0.002
1	< 10 <sup>-4</sup>	< 10 <sup>-4</sup>	0.025 ± 0.001	0.044 ± 0.002	0.030 ± 0.000
2	< 10 <sup>-4</sup>	< 10 <sup>-4</sup>	0.035 ± 0.000	0.085 ± 0.000	0.052 ± 0.002
3	< 10 <sup>-4</sup>	< 10 <sup>-4</sup>	0.038 ± 0.001	0.098 ± 0.000	0.054 ± 0.003
4	< 10 <sup>-4</sup>	0.036 ± 0.016	0.034 ± 0.007	0.070 ± 0.001	0.064 ± 0.003
6	< 10 <sup>-4</sup>	0.041 ± 0.008	0.012 ± 0.001	0.023 ± 0.001	0.058 ± 0.002

**Table 3**  
Separation factors for Y(III)/Sr(II) at different feed acidities.

HNO <sub>3</sub> , M	L-I	L-II	L-III	L-IV	L-V
0.01	> 49	> 318	> 563	> 920	3
0.1	> 130	> 6.3 × 10 <sup>4</sup>	347	> 5.9 × 10 <sup>4</sup>	131
0.5	> 3000	> 1.1 × 10 <sup>6</sup>	1.9 × 10 <sup>3</sup>	2.8 × 10 <sup>3</sup>	1.4 × 10 <sup>3</sup>
1	> 1.7 × 10 <sup>4</sup>	> 2.2 × 10 <sup>6</sup>	3.7 × 10 <sup>3</sup>	1.4 × 10 <sup>3</sup>	1.8 × 10 <sup>3</sup>
2	> 9.4 × 10 <sup>4</sup>	> 2.6 × 10 <sup>6</sup>	2.9 × 10 <sup>3</sup>	807	1.5 × 10 <sup>3</sup>
3	> 7.7 × 10 <sup>5</sup>	> 3.9 × 10 <sup>6</sup>	9.0 × 10 <sup>3</sup>	720	1.7 × 10 <sup>3</sup>
4	> 2.5 × 10 <sup>6</sup>	1.5 × 10 <sup>4</sup>	1.0 × 10 <sup>4</sup>	1.0 × 10 <sup>3</sup>	1.6 × 10 <sup>3</sup>
6	> 4.1 × 10 <sup>6</sup>	1.8 × 10 <sup>4</sup>	4.2 × 10 <sup>4</sup>	3.9 × 10 <sup>3</sup>	2.1 × 10 <sup>3</sup>



**Fig. 3.** Effect of feed acidity on the separation factors of Y(III)/Sr(II) by DGA-functionalized calix[4]arene ligands L-I–L-V; [Ligand] =  $1.0 \times 10^{-3}$  M, equilibration time: 1 h.

that obtained with T2EHDGA (Dutta et al., 2011b) as the extractant, clearly demonstrating the role of the calix[4]arene-based extractants in obtaining a higher selectivity for a particular metal ion. The higher S. F. values are attributed to a ‘cooperative action’ in the favourable extraction of Y(III). Furthermore, the crown ether like structure suggested (Dutta et al., 2012) for the extraction of Sr(II) is apparently lower with these ligands where the DGA arms are sitting on the calix [4]arene scaffold. On the other hand, the S.F. values were only 12 times larger than those obtained with PC-88A as the extractant (Table 4).

### 3.2. Nature of the extracted species

The extraction of  $Y^{3+}$  using diglycolamide extractants such as TODGA or T2EHDGA has been reported (Dutta et al., 2011a, 2011b)

**Table 4**  
Comparison of the separation factor values obtained in various solvent extraction methods.

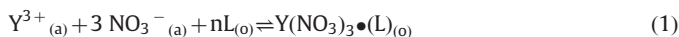
Extractant	S.F. (Y/Sr)	References
TODGA	> 60,000 <sup>a</sup>	Dutta et al. (2011a)
T2EHDGA	~600 <sup>b</sup>	Dutta et al. (2011a)
PC-88A	> 80,000 <sup>c</sup>	Kandwal et al. (2011)
DGA-functionalized calixarenes	> 10 <sup>6</sup>	Present work

<sup>a</sup> Feed: 6 M HCl.

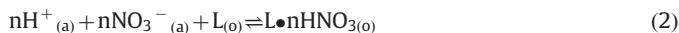
<sup>b</sup> Feed: 6 M HNO<sub>3</sub>.

<sup>c</sup> Feed: 0.1 M HNO<sub>3</sub>.

to follow a mechanism common to that of neutral extractants in the presence of a counter anion such as nitrate, as given below:



where (a) and (o) represent species in the aqueous and the organic phases, respectively, while L denotes the diglycolamide ligand. Due to a direct dependence of the metal ion transfer to the organic phase on the nitrate ion concentration, the above mentioned increase in the metal ion extraction occurred with increasing nitric acid concentrations. On the other hand, the plateau at higher concentrations of nitric acid can be attributed to a parallel adduct formation of the ligand with nitric acid as given below:



where *n* can be either 1 or 2. In case of the DGA-functionalized calix[4]arenes L-I–L-V, similar extraction equilibria are expected. The number of ligand molecules present in the extracted species can be obtained from an experiment wherein the distribution ratio of Y(III) is experimentally measured as a function of the concentration of the extractants. The *D<sub>Y</sub>* values can be correlated with the ligand concentration as indicated by Eq. (3):

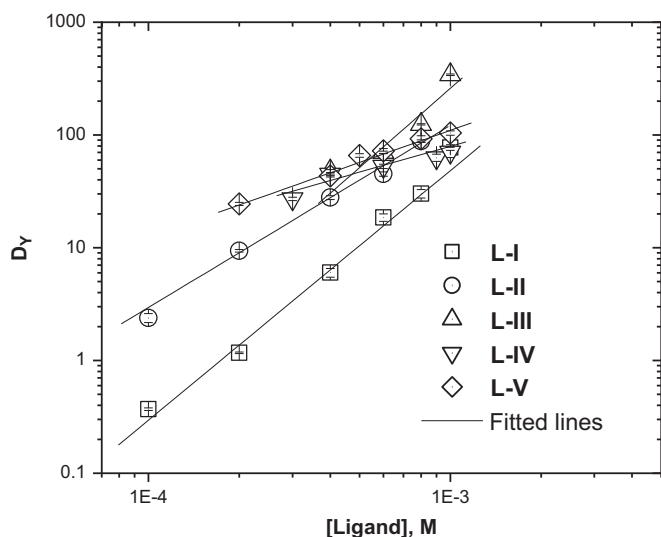
$$\log D = \log K_{ex} + 3 \log [NO_3^-] + n \log [L] \quad (3)$$

where *K<sub>ex</sub>* represents the two-phase extraction equilibrium constant for Eq. (1). The results of the ligand concentration variation studies in the form of log *D* vs log [*L*] plots are shown in Fig. 4, which gives straight line plots for all ligands. The slopes are also listed in Table 1. Only one ligand molecule was found to be associated for L-IV and L-V, while about two molecules were involved in the extraction of Y(III) in case of L-I and L-III. Though the stoichiometry in case of L-I and L-III was slightly higher than 2, extracted species containing three ligand molecules are highly improbable due to their large size. In case of L-II, however, a mixture of 1:1 and 1:2 species can be proposed. We have reported 1:2 species with L-I for Eu(III) extraction in a previous report (Raut et al., 2013). The nature of the species for Sr(II) extraction was not determined as the *D<sub>Sr</sub>* values were negligibly small in many cases.

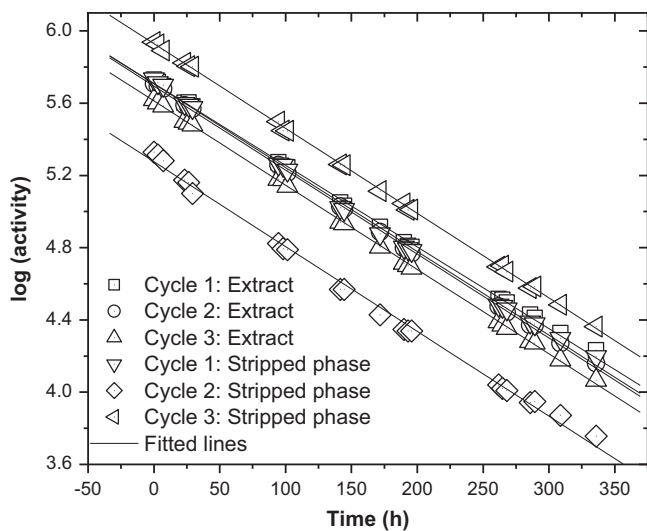
### 3.3. Separations of carrier-free <sup>90</sup>Y from a mixture of <sup>90</sup>Sr and <sup>90</sup>Y

The enormously large separation factor values obtained with the ligands L-I and L-II with individual radiotracers, brought us to carry out an actual separation of carrier-free <sup>90</sup>Y from a 1:1 mixture of <sup>90</sup>Sr and <sup>90</sup>Y. The followed protocol consisted of cycles of extraction and stripping and the stripped product containing predominantly <sup>90</sup>Y was subsequently tested for its purity. In view of the good stripping efficiency of EDTA from diglycolamide extracts (Dutta et al., 2011c), a  $1.0 \times 10^{-2}$  M solution of EDTA at pH 3 was used as the strippant solution.

A known amount of an <sup>90</sup>Y-<sup>90</sup>Sr mixture at an acidity of 3 M HNO<sub>3</sub> was used as the feed solution and was contacted with organic extractants ( $1.0 \times 10^{-3}$  M L-I and L-II in 95%



**Fig. 4.** Effect of ligand concentration on the distribution ratio of Y(III) by DGA-functionalized calix[4]arene ligands L-I-L-V; feed acidity: 3 M HNO<sub>3</sub>, equilibration time: 1 h.



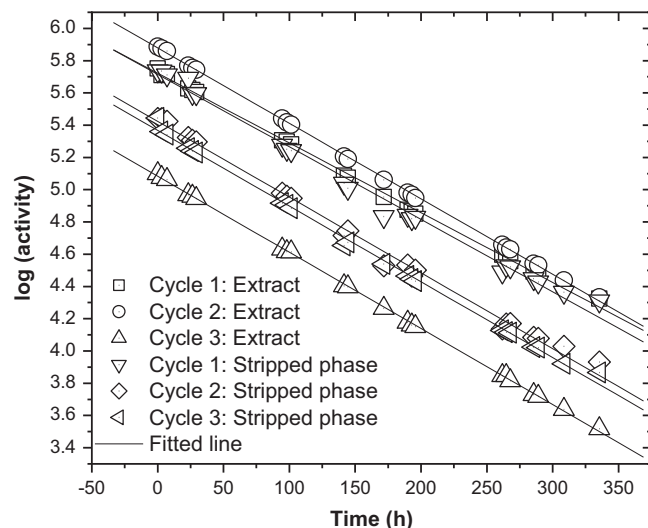
**Fig. 5.** Decay profiles of <sup>90</sup>Y product samples obtained at various stages of extraction and stripping. Feed solution: <sup>90</sup>Y-<sup>90</sup>Sr at 3 M HNO<sub>3</sub> ligand: L-I, diluent: 95% *n*-dodecane + 5% iso-decanol, strippant: 0.01 M EDTA at pH 3.

*n*-dodecane + 5% iso-decanol) followed by stripping with 0.01 M EDTA at pH 3. The stripped aqueous phase was dried and the feed acidity was adjusted to 3 M HNO<sub>3</sub> causing precipitation of EDTA, which was subsequently filtered off. The filtered solution was treated in the same manner for another cycle of extraction and stripping. In this manner three cycles were performed and samples were removed from the organic and the aqueous phases at each stage.

The purity of the product was ascertained from its half-life measurements over a period of several days. The decay profiles of the separated <sup>90</sup>Y for L-I and L-II are given in Figs. 5 and 6, respectively. The half-lives were calculated from the slope of the semi-log plot as follows:

$$\text{Half - life} = 0.301/\text{slope} \quad (4)$$

The half-lives of the products obtained after an extraction step and after a cycle of extraction and stripping for three consecutive cycles are listed in Table 5. As the results indicate, the extract



**Fig. 6.** Decay profiles of <sup>90</sup>Y product samples obtained at various stages of extraction and stripping. Feed solution: <sup>90</sup>Y-<sup>90</sup>Sr at 3 M HNO<sub>3</sub>, ligand: L-II, diluent: 95% *n*-dodecane + 5% iso-decanol, strippant: 0.01 M EDTA at pH 3.

**Table 5**

Half-lives of the products obtained during extraction of <sup>90</sup>Y from a <sup>90</sup>Y-<sup>90</sup>Sr mixture.

Extract fraction	Half-lives obtained (h)		Stripping fractions	Half-lives obtained (h)	
	L-I	L-II		L-I	L-II
Cycle 1	66.5	69.7	Cycle 1	64.8	66.9
Cycle 2	64.7	64.4	Cycle 2	64.4	64.1
Cycle 3	64.5	63.8	Cycle 3	64.1	64.1

phase invariably was contaminated, while the stripped phases yielded a better purity of <sup>90</sup>Y. L-II gave purer <sup>90</sup>Y products than L-I as the extractant. The final purity of the product was ascertained by allowing the <sup>90</sup>Y product to decay completely over a period of one month suggesting that the resultant counts (half the counts) will be due to the impurity in the form of <sup>90</sup>Sr while the other half of the counts were attributed to <sup>90</sup>Y resulting from the decay of <sup>90</sup>Sr. In a product sample containing about  $3 \times 10^5$  dpm of <sup>90</sup>Y, the final counts after one month were about 4 dpm which led to a decontamination factor (D.F.) of about  $10^5$ . This is reasonably high from this solvent extraction based separation method. However, in order to attain the required D.F. of  $10^6$ , one needs to couple with another separation method as reported previously (Dietz and Horwitz (1992)).

#### 4. Conclusions

DGA-functionalized calix[4]arenes L-I-L-V exhibit good extraction properties for Y(III) ions, while Sr(II) was poorly extracted. Especially L-I and L-II have separation factors of about  $10^6$  for Y(III) over Sr(II). Using the batch data obtained, a simple solvent extraction method was developed for the separation of carrier free <sup>90</sup>Y from a <sup>90</sup>Y-<sup>90</sup>Sr mixture. Pure <sup>90</sup>Y can be obtained after two cycles of extraction and stripping using L-I and L-II as extractants from 3 M HNO<sub>3</sub> feed with 0.01 M EDTA as strippant. The strongly complexing ligands will be very suitable for application in radiopharmaceuticals. The development of a low ligand inventory method like the use of a supported liquid membrane is under investigation. It is also planned to use ligands such as DTPA and

DOTA in the stripping solutions such that the stripped complexes of  $^{90}\text{Y}$  can be directly injected into the patients as the radiopharmaceutical.

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